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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/597,483	07/27/2006	Toru Mizushima	KPO-LTT-P6/LTT-99/US	1765

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EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
09/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/597,483	MIZUSHIMA ET AL.	
	Examiner	Art Unit	
	Paul Zarek	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9 and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/27/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 2-4 and 7 have been amended, Claims 17-19 have been added, and Claims 1, 10, 11, 15, and 16 have been cancelled by the Applicant in correspondence filed on 05/26/2009. Claims 2-9 and 17-19 are currently pending. This is the second Office Action on the merits of the claim(s).

REPSONSE TO ARGUMENTS

2. Examiner acknowledges receipt of English translations for Japanese patents 2003-207507, 7-171033A and 63-184063. The information contained therein has been considered. This is reflected in the outgoing PTOL-1449.

3. Claims 1-9, 15, and 16 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in light of Applicants' cancellation of Claims 1, 15, and 16.

4. Claims 1-6, 15, and 16 were rejected under 35 U.S.C. 102(b) as being anticipated by Jorgensen, et al. (US PreGrant Publication No. 2003/0175205). This rejection is moot in light of Applicants' cancellation of Claims 1, 15, and 16.

5. Claims 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jorgensen (above). This rejection is moot in light of Applicants' amendment to the rejected claims.

6. Newly added Claims 17-19 and amended Claims 2-9 are examined on their merits and the following **FINAL** rejection is made.

Claim Rejections - 35 USC § 112 (2nd paragraph)

7. The text of Title 35, U.S.C. § 112, second paragraph, can be found in a prior Office action.

8. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 recites the limitation "according to claim 1" in line 1. There is insufficient antecedent basis for this limitation in the claim because Claim 1 has been cancelled by Applicant. For prior art search purposes, Examiner interprets Claim 9 to depend from newly added Claim 17.

Claim Rejections - 35 USC § 103

9. The text of Title 35, U.S.C. § 103(a) can be found in a prior Office action.

10. Claims 2-9 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jorgensen, et al. (US PreGrant Publication no. 2003/01752058, already of record), in view of Smale and Bjarnason (British Journal of Clinical Pharmacology, 2003).

11. Newly added Claim 17 (from which Claims 2-9 depend) is drawn to a screening assay comprising:

(a) preparing liposomes formed from phospholipid and encapsulate a fluorescent dye;
(b) allowing a test compound and at least one compound of known gastric toxicity to separately react with the liposome;
(c) measuring the leakage of the fluorescent dye from the liposome; and,
(d) comparing the leakage caused by the test compound to the leakage caused by the compound(s) of known gastric toxicity.

Claim 2 limits the phospholipid (e.g. phosphotidylcholine). Claim 3 further limits the method such that the evaluation of dye leakage (step c) is accomplished by measuring the emitted wavelength of the dye. Claims 4 and 5 limit the dye (e.g. calcein). Claim 6 further limits the method of Claim 5 such that the fluorescence of the calcein is measured at 520 nm. Claims 7-9 limit the test compound to anti-inflammatory compounds (Claim 7), NSAIDs or steroids (Claim 8), or a compound that acts to protect gastric mucosa (Claim 9). Claim 18 is drawn to a screening assay similar to that of Claim 17, with the test compound being an NSAID. Claim 19 is drawn to a screening assay similar to that of Claim 17, with the difference being that the test compound and the known compound of gastric toxicity react with the liposome together to determine the gastric protective effects of the test compound.

12. Jorgensen, et al., teach a screening assay in which prepared liposomes comprising phosphaditylcholine are made to encapsulate calcein (paragraph 0180). The lysis of the liposome by a test compound (e.g. snake venom PLA_2) resulted in the leakage of calcein from the liposome (paragraph 0181). The evaluation of calcein leakage was performed by exciting the calcein by light at wavelength of 492 nm, and measuring the fluorescent intensity at 520 nm (paragraph 0180 and 181). Jorgensen, et al., however, do not contemplate anti-inflammatory compounds or gastric mucosa-protecting compounds as the test compound or comparing a test compound to that of known gastric toxicity.

13. Smale and Bjarnason teach that the topical toxicity (in the GI tract) of NSAIDs "may relate to their detergent action, which includes the interaction between the NSAIDs and surface membrane phospholipids" (pg 285, col 2, para 5, lines 1-4). Thus, Smale and Bjarnason provide

motivation for a skilled artisan to assay NSAIDs for their effect on cell-free phospholipid membranes.

14. The reference of Jorgensen, et al., toward the effect of snake venom PLA_2 or tumor imaging is not relevant to the applicability of this art to the claims. One of ordinary skill in the art would reasonably recognize that the cell-free system disclosed in Jorgensen, et al., would be useful for the determination of gastric toxicity of NSAIDs, given the mechanism of action of gastric toxicity of the NSAIDs (e.g. disruption of the phospholipid membrane). Furthermore, although Jorgensen, et al., does not disclose comparing a test compound to a reference compound, such comparisons are routine in the art and this control would be within the purview of the skilled artisan. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to screen NSAIDs, or other compounds with gastric toxicity, with the assay disclosed by Jorgensen, et al.

Conclusion

15. Claims 2-9 remain rejected. Claims 17-19 are rejected.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/San-ming Hui/
Primary Examiner, Art Unit 1617